## PATENT COOPERATION TREATY

# **PCT**

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Artcle 36 and Rule 70)

| Applicant's or agent's file reference   |   |  |                                     |  |  |  |
|---|---|--|-------------------------------------|--|--|--|
| PCTA9407-2  | FOR FURTHER AC  | TION   | See Form PCT/IPEA/416               |  |  |  |
| International application No. International filing date(  |   | day/month/year)                                  | Priority date (day/month/year)      |  |  |  |
| PCT/KR2004/001819   | 21 JULY 2004 (21.   | 07.2004)   | 30 JANUARY 2004 (30.01.2004)        |  |  |  |
| International Patent Classification (IPC)  C12N 15/54(2006.01)i, C12N 1  Applicant  | •   |  |                                     |  |  |  |
| Korea Research Institute of B   |   |  |                                     |  |  |  |
| This report is the international pro-<br>Authority under Article 35 and tra   | eliminary examination repeats ansmitted to the applicant  | ort, established by this according to Article 36 | International Preliminary Examining |  |  |  |
| 2. This REPORT consists of a total  | of 6 sheets   | , including this cover s                         | heet.                               |  |  |  |
| 3. This report is also accompanied by ANNEXES, comprising:  a. (sent to the applicant and to the International Bureau) a total of sheets, as follows:  sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the  |   |  |                                     |  |  |  |
| Administrative Instructions).  sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.  b. (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions). |   |  |                                     |  |  |  |
| 4. This report contains indications re  Box No. I Basis of the  |   | ms:  |                                     |  |  |  |
| Box No. II Priority   |   |  |                                     |  |  |  |
| Box No. III Non-establi   |   |  |                                     |  |  |  |
|   |   |  |                                     |  |  |  |
| Box No. V Reasoned s citations and  | Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |  |                                     |  |  |  |
| Box No. VI Certain doc  | uments cited  |  |                                     |  |  |  |
| Box No. VII Certain defects in the international application  |   |  |                                     |  |  |  |
| Box No. VIII Certain observations on the international application  |   |  |                                     |  |  |  |
| Date of submission of the demand  |   | Date of completion of this report                |                                     |  |  |  |
| 26 OCTOBER 2005 (26.10.2005)  |   | 18 MAY 2006 (18.05.2006)                         |                                     |  |  |  |
| Name and mailing address of the IPEA/   |   | Authorized officer                               | m 2006. 5. 24 E                     |  |  |  |
| Korean Intellectual Property Office<br>920 Dunsan-dong, Seo-gu, Daejeon 302-701,<br>Republic of Korea   |   | KIN, Ji Yun                                      | (RISIN)                             |  |  |  |
| Facsimile No. 82-42-472-7140  |   | Telephone No. 82-42                              | 2-481-8288                          |  |  |  |

#### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/KR2004/001819

## Box No. I Basis of the report 1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item. which is the language of a translation furnished for the purposes of: international search (under Rules 12.3 and 23.1(b)) publication of the international application (under Rule 12.4) international preliminary examination (under Rules 55.2 and/or 55.3) 2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this reort as "originally filed" and are not annexed to this report): the international application as originally filed/furnished the description: pages as originally filed/furnished pages\* received by this Authority on pages\* received by this Authority on the claims: pages as originally filed/furnished pages\* as amended (together with any statment) under Article 19 received by this Authority on pages\* pages\* \_\_\_\_ received by this Authority on the drawings: pages . \_as originally filed/furnished pages\* received by this Authority on pages\* received by this Authority on the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing. The amendments have resulted in the cancellation of: the description, pages \_\_ the claims, Nos. the drawings, sheets the sequence listing (specify): any table(s) related to sequence listing (specify): 4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)). the description, pages the claims, Nos. \_ the drawings, sheets the sequence listing (specify): \_ any table(s) related to sequence listing (specify): \* If item 4 applies, some or all of those sheets may be marked "superseded."

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/KR2004/001819

| Box No. III Non-establishment of opinion with regard to novelty, inventive step and industria  | l applicability                       |
|--|---------------------------------------|
| The questions whether the claimed invention appears to be novel, to involve an inventive step (to be applicable have not been examined in respect of:  | e non obvious), or to be industrially |
| the entire international application,  |                                       |
| claims Nos. 11   |                                       |
| because:   |                                       |
| the said international application, or the said claims Nos.  |                                       |
| relate to the following subject matter which does not require an international preliminary ex-   | amination (specify):                  |
|  | •                                     |
| · ·  | •                                     |
|  |                                       |
|  |                                       |
| ,  | •                                     |
| the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):  |                                       |
|  |                                       |
| , and the second se   |                                       |
|  |                                       |
|  |                                       |
|  |                                       |
| the claims, or said claims Nos.  | are so inadequately supported         |
| by the description that no meaningful opinion could be formed (specify):   |                                       |
|  |                                       |
|  |                                       |
|  |                                       |
|  |                                       |
| no international search report has been established for said claims Nos. 11  |                                       |
| a meaningful opinion could not be formed without the sequence listing; the applicant did not,  | within the prescribed time limit:     |
| furnish a sequence listing on paper complying with the standard provided for in Annex C  |                                       |
| Istructions, and such listing was not available to the International Preliminary Examining   | Authority in a form and               |
| manner acceptable to it.  furnish a sequence listing in electronic form complying with the standard provided for in A  | Annex C of the Administrative         |
| Istructions, and such listing was not available to the International Preliminary Examining   | Authority in a form and               |
| manner acceptable to it.  pay the required late furnishing fee for the furnishing of a sequence listing in response to a 13ter.1(a) or (b) and 13ter.2.  | n invitation under Rule               |
| a meaningful opinion could not be formed without the tables related to the sequence listings;  | Alexandrana did ana didit d           |
| prescribed time limit, furnish such tables in electronic form complying with the technical required C-bis of the Administrative Instructions, and such tables were not available to the Internation Authority in a form and manner acceptable to it. | uirements provided for in Anney       |
| the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form on technical requirements provided for in Annex C-bis of the Administrative Instructions.   | ly, do not comply with the            |
| See Supplemental Box for further details.  | •                                     |

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### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/KR2004/001819

| Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; |
|-----------|--|
|           | citations and explanations supporting such statement   |

| 1. | Statement                     |        |        |     |
|----|-------------------------------|--------|--------|-----|
|    | Novelty (N)                   | Claims | 1-10   | YES |
|    | ·                             | Claims | None   | No  |
|    | Inventive step (IS)           | Claims | 1-10   | YES |
|    |                               | Claims | None   | NO  |
|    | Industrial applicability (IA) | Claims | 1-10 · | YES |
|    | •                             | Claims | None   |     |

- 2. Citations and explanations (Rule 70.7)
  - (1) The following documents have been considered for the purpose of this report;

D1: Proc. Nat'l. Acad. Sci. Vol. 100, pp. 5022-5027 (April 2003)

D2: Glybiology, Vol. 5, pp. 671-681 (1995)

D3: J. Biol. Chem., Vol. 273, pp. 26298-26304 (October 1998)

D4: J. Biol. Chem. Vol. 268, pp. 26338-26345 (December 1993)

D5: US 2004/0137134 A (26 September 2002)

D6: KR 2004/0004089 (13 January 2004)

(2) Novelty and Inventive Step

The present invention relates to a novel  $\alpha$ -1,6-mannosyltransferase gene from *Hansenula polymorpha* which codes for enzyme initiating outer chain elongation in N-linked glycosylation. It also discloses a process for producing a glycoprotein without human incompatible sugar chain using  $\alpha$ -1,6-mannosyltransferase deficient mutant of H. polymorpha.

Claims 1–7 relate to a nucleic acid encoding a protein of an amino acid according to SEQ ID No. 2 or a protein with  $\alpha$ -1,6-mannosyltransferase activity having an amino acid at least 90% homologous to SEQ ID No. 2, a protein coded by said nucleic acid, a recombinant vector comprising a nucleic acid according to SEQ ID No. 1(KCTC 10583BP), and a *H. polymorpha* mutant strain having a deficiency in the  $\alpha$ -1,6-mannosyltransferase gene(KCTC 10584BP). Claims 8–10 relate to a process for producing a glycoprotein with reduced glycosylation using said mutant yeast.

(Continued on Supplemental Sheet.)

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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| Supplemental Box Relating to Sequence Listing   |
|---|
| Continuation of Box No. I, item 2:  |
| 1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:   |
| a. type of material  a sequence listing table(s) related to the sequence listing  |
| b. format of material on paper in electronic form   |
| c. time of filing/furnishing  contained in the international application as filed  filed together with the international application in electronic form  furnished subsequently to this Authority for the purposes of search and/or examination   |
| received by this Authority as an amendment* on  2. In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed of furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. |
| 3: Additional comments:   |
|   |
|   |

PCT/KR2004/001819

#### Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of:

Box No. V

D1 to D5 disclose  $\alpha$ -1,6-mannosyltransferases from various yeast strains. In addition, the documents also disclose that  $\alpha$ -1,6-mannosyltransferase can be used for producing glycoengineered protein, especially characterized by having a structure of Man5GlcNac2 and Man8GlcNAc2.

D5 and D6 disclose a method for producing glycoproteins having a similar glycosylation pattern to the one produced in human by introducing a gene encoding enzyme involved in glycosylation including  $\alpha$ -1,6-mannosyltransferase.

However, the documents set forth above do not provide any amino acid or nucleotide sequence with significant homology to the sequences provided in this invention, or fairy suggest a mutant deficient in  $\alpha$ -1,6-mannosyltransferase gene and a method of production of glycoprotein using said mutant.

Thus, claims 1-10 are novel and involve an inventive step [PCT Article 33(2) and 33(3)].

(3) Industrial Applicability

The subject matter of claims 1-10 is considered to be industrially applicable under PCT Article 33(4).